UPDATE
National Toxicology Program

July 2007

Headquartered at the National Institute of Environmental Health Sciences NIH-DHHS

What's Inside:

John Bucher Chosen to Head NTP

Article by Eddy Ball, reprinted from eFactor, July 2007

On June 15, NIEHS announced the appointment of toxicologist John Bucher, Ph.D., as associate director of the National Toxicology Program (NTP). Bucher has been a part of the NTP for 24 years, most recently as deputy director of the Environmental Toxicology Program and chief of its Toxicology Operations Branch.

Selected from a group of 33 qualified applicants for the position, Bucher began his new duties on June 18, as the program started a process of realignment within the Institute's Division of Intramural Research. He succeeds Allen Dearry, Ph.D., who served as acting associate director from January 2006 to June 2007.

In announcing the choice, NIEHS Director and Director of the NTP David A. Schwartz, M.D., praised Bucher as a scientist with "outstanding scientific credentials, an insightful vision for toxicological research and an in-depth knowledge of the NTP." Schwartz expressed his confidence in Bucher's ability to realize the goals of the NTP Vision and Roadmap for the 21st century, which the new associate director was instrumental in developing.

Bucher joined the NTP in September 1983 after completing his Ph.D. in Pharmacology at the University of Iowa and a postdoctoral fellowship at Michigan State University. He has served as chief of the Toxicology Operations Branch for the past 11 years and deputy director of the Environmental Toxicology Program since 1995. Bucher received his certification as a diplomate by the American Board of Toxicology in 1984.

During his tenure at NTP/NIEHS, Bucher has published over 100 studies in peer-reviewed journals and played a key role in shaping the program's research and policies, including comprehensive studies of dioxin and dioxin-like chemicals, chemicals that mimic estrogens and, more recently as one of the pioneers

(Photo courtesy of Steve McCaw)

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Dr. Susan A Elmore Awarded *Best Paper Award* for 2006

Congratulations to Susan A. Elmore, MS, DVM, DACVP, and NTP Pathologist/Staff Scientist, for winning the *Best Paper Award* for 2006 by the Society of Toxicologic Pathology (STP). The award was presented at the Annual Meeting Awards Ceremony at the STP Annual Meeting on Wednesday evening, June 13, 2007, in Rio Grande, Puerto Rico.

The article "The Transduction of Rat Submandibular Glands by an Adenoviral Vector Carrying the Human Growth Hormone Gene is Associated with Limited and Reversible Changes at the Infusion Site" was published in the journal *Toxicologic Pathology* (34:385-392, 2006). Coauthors are Linda Lanning (Otsuka Maryland Research Institute), Neil Allison (Experimental Pathology Laboratory), Molly Vallant (Environmental Toxicology Program, NIEHS) and Abraham Nyska (Integrated Laboratory Systems). The paper documents the findings of the pathology evaluation of a NTP study that evaluated the use of adenoviral vectors to deliver exogenous genes to submandibular salivary glands. The ultimate goal is to correct protein deficiencies through

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NEXT

Upcoming Events

August 6-8, 2007
Second Meeting of the CERHR
Expert Panel on Bisphenol A
Hilton Alexandria Old Town, 1767 King Street
Alexandria, VA 22314

December 6, 2007
NTP Board of Scientific Counselors
National Institute of Environmental Health Sciences
111 T.W. Alexander Drive
Research Triangle Park, NC 27709

http://ntp.niehs.nih.gov/go/calendar

New NIEHS Seminar Series Launches

NIEHS has begun a new weekly seminar series, Frontiers in Environmental Sciences. The series will feature cutting-edge research aimed at the broad scientific interests of the NIEHS research community. Many of the speakers will be current and/or former NIEHS grantees. The talks will come mostly from local scientists and will offer the opportunity for new collaborations and expansion of our own research interests. Lectures are available in streaming video and iTunes/iPod compatible video or enhanced video. ●
http://www.niehs.nih.gov/news/video/science/frontiers/

Dr. Robert Sills appointed Chief, Laboratory of Experimental Pathology

Dr. Robert Sills has been appointed to the Senior Scientist position of Chief, Laboratory of Experimental Pathology, Environmental Toxicology Program, NIEHS. Dr. Sills replaces Dr. Bob Maronpot, who recently retired. Please join us in congratulating Dr. Sills, and supporting him as he takes on this important responsibility. Dr. Dave Malarkey, Laboratory of Experimental Pathology, had been serving as acting laboratory chief until Dr. Sills' appointment. ●

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John Bucher Chosen to Head NTP

in the field, manufactured nanomaterials. Bucher's leadership was important in the development of the NTP Center for the Evaluation of Risks to Human Reproduction.

"I look forward to working with our exceptionally talented staff and NTP partners to produce the quality data and scientific understanding necessary for the protection of public health and critical to the further evolution of the science of toxicology," said Bucher. "I am honored to follow in the footsteps of the truly outstanding individuals who have led this program in the past."

According to Schwartz, realignment of the NTP within DIR will help it achieve higher visibility and greater efficiency. "Our goal is to closely coordinate NTP and DIR research so we can make the most of our resources and have an even greater impact on safeguarding public health," Schwartz said. ●

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Dr. Susan A Elmore Awarded *Best Paper Award* for 2006

the expression of a transgene coding for the required protein with therapeutic and sustained levels of transgene-encoded proteins in the bloodstream.

Dr. Elmore's award honors the author of a work of exceptional merit dealing with a subject related to the Society's technical scope, and appearing in the journal, irrespective of the author's age. The paper was selected on the basis of general quality, originality, subject matter, and timeliness, while also representing a significant advance in the presentation of a new concept or method with important applications. The paper must be well written, clearly illustrated, and referenced comprehensively. In addition, the expectation is that the article will be cited frequently, and for many years, in the literature. All authors will share a monetary prize of $1000 and plaques were awarded to the individual authors. The NTP is proud and honored to have such scientists as members of its staff potential. ●

NTP Board of Scientific Counselors

Upcoming BSC Meeting
The next NTP Board of Scientific Counselors Meeting will be held on December 6, 2007, at the NIEHS in Research Triangle Park, NC. Preliminary agenda items include NTP study nominations, a presentation of a concept review for studies on mold, and a report from the Technical Reports Review Subcommittee on their recommendations following peer review of seven draft NTP Technical Reports reviewed on May 16-17, 2007. ● http://ntp.niehs.nih.gov/go/calendar

Review of NTP Contracts
A working group of the NTP Board of Scientific Counselors (BSC) conducted a review of NTP contracts to (1) assess potential conflicts of interest, (2) consider what recommendations might be appropriate to reduce the potential for COI to occur, and (3) address how to mitigate any current or future COI. The working group report was presented to the NTP BSC at its meeting on June 22 at the NIEHS. Following its discussion, the BSC accepted the report unanimously without revision. The report is posted on the NTP web site. ●
http://ntp.niehs.nih.gov/go/9741

The NTP Board of Scientific Counselors Technical Reports Review Subcommittee

May 2007 Peer Review
The Technical Reports Review Subcommittee of the NTP Board of Scientific Counselors met on May 16-17, 2007, at the NIEHS, Research Triangle Park, NC to peer review the findings and conclusions from draft NTP technical reports using conventional rodent models. The subcommittee made the recommendations recorded below regarding the findings and conclusions of the reports. These findings will be reported to the NTP Board of Scientific Counselors at its meeting on December 6, 2007. Additional details about the meeting are available on the NTP web site.
http://ntp.niehs.nih.gov/go/15849

Sodium dichromate dihydrate (TR 546)
The subcommittee accepted unanimously (6 yes, 0 no) the conclusions as written, *clear evidence of carcinogenic activity* of sodium dichromate dihydrate in male and female F344/N rats and *clear evidence of carcinogenic activity* in male and female B6C3F1 mice.

Formamide (TR 541)
The subcommittee accepted unanimously (6 yes, 0 no) the conclusions, *no evidence of carcinogenic activity* of formamide in male and female F344/N rats, *clear evidence of carcinogenic activity* in male B6C3F1 mice, and equivocal evidence of carcinogenic activity in female B6C3F1 mice. The subcommittee recommended that bone marrow hyperplasia in male rats was associated with exposure to formamide.

Ethinyl estradiol (multigenerational study) (TR 547)
The subcommittee accepted unanimously (6 yes, 0 no) the summary of the findings for this continuous breeding study. The subcommittee recommended deleting that treatment related effects may have been carried over to the unexposed F4 generation and that the estrous cycle time was not prolonged at the lowest exposure concentration of 2 ppb. It should be noted that offspring from the F1 and F3 generations exposed *in utero* and during lactation to ethinyl estradiol were either exposed to ethinyl estradiol or a control diet until 2 years of age (TR 545).

Ethinyl estradiol (2-year bioassay) (TR 548)
The subcommittee accepted unanimously (7 yes, 0 no) the conclusions as written, *no evidence of carcinogenic activity* in F1 male or female Sprague-Dawley rats exposed to ethinyl estradiol from conception to 2 years of age, *no evidence of carcinogenic activity* in F1 male Sprague-Dawley rats, and equivocal evidence of carcinogenic activity in F1 female Sprague-Dawley rats exposed to ethinyl estradiol from conception to 20 weeks of age followed by control diet to 2 years of age.

The subcommittee accepted unanimously (7 yes, 0 no) the conclusions, *equivocal evidence of carcinogenic activity* in F3 female Sprague Dawley rats exposed to ethinyl estradiol from conception through weaning at postnatal day 21 followed by control diet to 2 years of age. The subcommittee recommended *equivocal evidence of carcinogenic activity* in F3 male Sprague Dawley rats exposed to the same treatment regimen.

Cumene (TR 542)
The subcommittee accepted unanimously (6 yes, 0 no) the conclusions, *clear evidence of carcinogenic activity* of cumene in male F344/N rats, *some*

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evidence of carcinogenic activity in female F344/N rats, and *clear evidence of carcinogenic activity* in male and female B6C3F1 mice. The subcommittee recommended adding that the increased incidences of interstitial cell adenomas of the testes in male rats and the increased incidences of hemangiosarcoma of the spleen and follicular cell adenoma in male mice may have been related to cumene exposure. The subcommittee stated that the nonneoplastic lesions in the kidney in male rats are characteristic of α2u-globulin accumulation.

Cresols (TR 550)
The subcommittee accepted unanimously (6 yes, 0 no) the conclusions as written, *equivocal evidence of carcinogenic activity* of 60:40 m/p-cresol in male F344/N rats and *some evidence of carcinogenic activity* in female B6C3F1 mice.

Propargyl alcohol (TR 552)
The subcommittee accepted (4 yes, 2 no) the conclusions, *some evidence of carcinogenic activity* of propargyl alcohol in male F344/N rats, and *no evidence of carcinogenic activity* in female F344/N rats. The subcommittee recommended *some evidence of carcinogenic activity* in male and female B6C3F1mice.

The NTP Board of Scientific Counselors Technical Reports Review Subcommittee will meet on February 27-28, 2008, at the NIEHS, 111 T.W. Alexander Drive, Research Triangle Park, NC to peer review the findings and conclusions from 6 draft NTP Technical Reports performed in conventional rodent models. A seventh draft report is on studies of the photocarcinogenicity of aloe vera conducted in the SKH-1 mouse. A 90-day draft NTP Toxicity Report on estragole (TOX 82) will also be reviewed. NTP is making tentative plans to present two draft reports on toxicogenomic studies.

The draft reports tentatively scheduled for review are:

TR-544	Dibromoacetonitrile
TR-553	Photocarcinogenicity study of aloe vera
TR-549	Bromochloroacetic acid
TR-555	1,2-Dibromo-2,4-dicyanobutane
TR-551	Isoeugenol
TR-556	Chromium picolinate monohydrate
TR-554	5-(Hydroxymethyl)-2-furfural
TOX-82	Estragole

Details about this meeting are at web site http://ntp.niehs.nih.gov/go/calendar or can be obtained by contacting the Executive Secretary, Dr. Barbara Shane. This meeting is open to the public and public comment, both written and oral, is welcome on any report.

Contact Information: Dr. Barbara Shane, Executive Secretary, NTP Liaison and Scientific Review Office, NIH/NIEHS, P.O. Box 12233, MD A3-01, Research Triangle Park, NC 27709; T: 919- 541-4253; shane@niehs.nih.gov

NTP Center for the Evaluation of Risks to Human Reproduction (CERHR)

Second Bisphenol A Expert Panel Meeting
The NTP CERHR convened an independent 12-member expert panel of scientists to evaluate bisphenol A on March 5-7, 2007, in Alexandria, Virginia. This panel evaluated information on human exposure and the reproductive and developmental toxicity of bisphenol A. Bisphenol A is a high production volume chemical used in the production of epoxy resins, polyester resins, polysulfone resins, polyacrylate resins, polycarbonate plastics, and flame retardants. The meeting summary can be found on the CERHR web site for bisphenol A. http://cerhr.niehs.nih.gov/chemicals/bisphenol/bisphenol.html The expert panel did not complete its evaluation at the March meeting; therefore, a second meeting of the expert panel will be held on August 6-8, 2007, at the Hilton Alexandria Old Town 1767 King Street, Alexandria, VA 22314 (72 FR 33228). The interim draft report, public comments received on this draft, and other information about the meeting are available on the web site. This meeting is open to the public and time will be set-aside on August 6 for oral public comments.

NTP is undertaking an audit of the literature cited in the draft CERHR expert panel reports on bisphenol A and the fidelity of requested changes to the reports. Upon completion of the audit, the report will be available on the CERHR web site for bisphenol A.

Contact Information: Dr. Michael D. Shelby, Director CERHR, NIH/NIEHS, P.O. Box 12233, MD EC-32, Research Triangle Park, NC 27709, T: (919) 541-3455; FAX: (919) 316-4511 shelby@niehs.nih.gov

NTP Testing Program

Request for Study Nominations

With a broad mandate to provide toxicological characterizations for chemicals and other substances of public health concern, the NTP accepts nominations for new toxicological studies at any time. Labor unions, academic scientists, federal and state agencies, industry, and the general public are welcome to make nominations for specific substances or for general issues related to potential human health hazards of occupational or environmental exposures. As available, a rationale for study should accompany the nomination along with background information describing sources of exposure and possible adverse health effects or concerns associated with exposure, the chemical name and the Chemical Abstract Service (CAS) registry number. Details about the nomination review and selection process are available on the NTP web site http://ntp.niehs.nih.gov (select Nominations to the Testing Program under the heading Testing Information) or by contacting the NTP Office of Chemical Nomination and Selection (contact information below).

Current areas of focus in the NTP's testing program include potential hazards associated with radiofrequency radiation from cellular phones, nanoscale materials, perfluorinated compounds, herbal dietary supplements, photoactive chemicals, brominated flame retardants, certain complex occupational exposures, dioxin-like compounds, contaminants of finished drinking water, and endocrine-disrupting substances.

All nominations undergo several levels of review before being selected by the NTP for study. These steps of review help to ensure that the NTP's testing program addresses toxicological concerns pertinent to all areas of public health and helps maintain balance among the types of substances and issues evaluated. Studies are initiated on selected nominations as time and resources permit.

Study Nominations Currently in Review

A Federal Register notice published on March 29, 2007, formally solicited comment on the nine new nominations and corresponding preliminary study recommendations listed in next column (72 FR 14816).

Supporting documents and public comments received for these nominations are available on the NTP web site at http://ntp.niehs.nih.gov/go/29287
Four of these new study nominations were reviewed by the NTP Board of Scientific Counselors (BSC) at a public meeting on June 22, 2007: artificial butter flavoring mixture and certain components; naturally occurring asbestos; nanoscale silver; and o-phthalaldehyde. The remaining nominations will be reviewed by the BSC at the next scheduled meeting. Information related to the June 22 meeting is available on the NTP web site at http://ntp.niehs.nih.gov/go/9741
Questions or comments on any of the new study nominations should be directed to Dr. Scott Masten.

- **Aminopyridines (2-Aminopyridine, 3-Aminopyridine, 4-Aminopyridine):** Recommended studies – Toxicological characterization including chronic toxicity and carcinogenicity studies for 2-aminopyridine; short-term mechanistic studies for 3- and 4-aminopyridine; comparative neurotoxicity studies for 2-, 3-, and 4-aminopyridine
- **Artificial butter flavoring mixture and certain components, acetoin and diacetyl:** Recommended studies – Chronic toxicity and carcinogenicity studies via inhalation; mechanistic studies
- **Asbestos, naturally occurring and atypical forms:** Recommended studies – Mineral characterization; *in vitro* durability and toxicity studies; subchronic and chronic toxicity/ carcinogenicity studies via inhalation; studies should utilize test materials representative of minerals identified in Libby, MT and at other Naturally Occurring Asbestos (NOA) sites
- **Diethyl phthalate:** Recommended studies – Multigeneration oral reproductive and developmental toxicity studies; toxicokinetic studies (oral and dermal routes)
- **2',2"-Dithiobisbenzanilide:** Recommended studies – Genotoxicity and metabolism studies
- **2-Methoxy-4-nitroaniline:** Recommended studies – Toxicological characterization; short-term mechanistic studies to predict carcinogenic potential

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NTP Interagency Center for the Evaluation of Alternative Toxicology Methods (NICEATM)

Draft NICEATM-ICCVAM Five-Year Plan: Status Update
Congress has requested that NICEATM and the Interagency Coordinating Committee for the Validation of Alternative Methods (ICCVAM) in partnership with the relevant federal agencies develop a five-year plan that addresses (1) research, development, translation, and validation of new and revised non-animal and other alternative assays for integration into federal agency testing programs and (2) the identification of areas of high priority for new and revised non-animal and alternative assays for the replacement, reduction, and refinement (less pain and distress) of animal tests. On May 7, 2007, a draft version of this document was released for public comments to be considered by NICEATM, ICCVAM, and agency program offices in finalizing the plan. The request for public comments was announced in Federal Register (72 FR 23832).

On June 11, 2007 a Town Meeting was held to describe the draft plan and receive oral comments from the public. Over 60 people attended the meeting, which was held at Natcher Conference Center of the National Institutes of Health in Bethesda, MD. The Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) met the following day, June 12, 2007, to provide a summary of its review of the draft plan, recommendations for incorporation into the final document, and an additional opportunity for public comment. The report prepared by a working group of SACATM and discussed at the meeting is available on the meeting web site http://ntp.niehs.nih.gov/go/8202

The draft Five-Year Plan and the public comments received can be viewed at the ICCVAM-NICEATM Five-Year Plan web site.
http://iccvam.niehs.nih.gov/docs/5yearplan.htm

Availability of Independent Peer Review Panel Report on Five *In Vitro* Pyrogen Test Methods
NICEATM announced the availability of the Independent Peer Review Panel Report: Five *In Vitro* Test Methods Proposed for Assessing Potential Pyrogenicity of Pharmaceuticals and Other Products ion May 9 (72 FR 26396). NICEATM in collaboration with ICCVAM convened an independent scientific peer review panel meeting on February 6, 2007, to evaluate the validation status of five in vitro pyrogen test methods proposed as replacements for the Rabbit Pyrogen Test (RPT). The peer review panel report from this meeting is now available. The report contains (1) the panel's evaluation of the validation status of the methods and (2) the panel's comments and conclusions on draft ICCVAM test method recommendations. NICEATM invited public comment on the panel's report and the report, public comments received, and additional information may be viewed on the NICEATM/ICCVAM web site at http://iccvam.niehs.nih.gov/methods/pyrogen/pyrogen.htm

Request for Comments, Nominations of Scientific Experts, and Submission of Data on the Use of the Murine Local Lymph Node Assay
NICEATM and ICCVAM received a nomination from the U.S. Consumer Product Safety Commission (CPSC) to evaluate the validation status of: (1) the murine local lymph node assay (LLNA) as a stand-

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NTP Testing

- **Nanoscale gold and nanoscale silver:** Recommended studies – materials characterization; metabolism and pharmacokinetic studies; acute, subacute and subchronic toxicity studies; mechanistic studies to assess the role of size and surface coating on biological disposition and toxicity
- **o-Phthalaldehyde:** Recommended studies – Toxicological characterization including studies to assess dermal irritation, dermal toxicity, and sensitization and asthmagenic potential
- **Pentaethylenehexamine:** No studies at this time due to the irritant and corrosive nature of this compound ●

Contact Information: Dr. Scott A. Masten, Director, Office of Chemical Nomination and Selection, NIH/NIEHS, P. O. Box 12233, MD A3-07, Research Triangle Park, North Carolina 27709; T: 919- 541-5710; FAX: 919-541-3647; masten@niehs.nih.gov

NTP Staff Publications: January-May 2007

The names of NIEHS/NTP staff are identified in bold. The URL to the article is provided although in some incidences, access may require a subscription to the journal.

Burlinson, B., **R. R. Tice**, G. Speit, E. Agurell, S. Y. Brendler-Schwaab, A. R. Collins, P. Escobar, M. Honma, T. S. Kumaravel, M. Nakajima, Y. F. Sasaki, V. Thybaud, Y. Uno, M. Vasquez and A. Hartmann (2007). "Fourth International Workgroup on Genotoxicity Testing: Results of the *in vivo* Comet assay workgroup." *Mutation Research-Genetic Toxicology and Environmental Mutagenesis.* **627**(1): 31-35.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244081300004

Carey, M. A., J. W. Card, J. A. Bradbury, M. P. Moorman, N. Haykal-Coates, S. H. Gavett, L. P. Graves, V. R. Walker, **G. P. Flake**, J. W. Voltz, D. L. Zhu, E. R. Jacobs, A. Dakhama, G. L. Larsen, J. E. Loader, E. W. Gelfand, **D. R. Germolec**, K. S. Korach and D. C. Zeldin (2007). "Spontaneous airway hyperresponsiveness in estrogen receptor-alpha-deficient mice." *American Journal of Respiratory and Critical Care Medicine.* **175**(2): 126-135.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000243508500006

Cesta, M. F., J. P. Davis and **M. L. Cunningham** (2007). "Detection of quantum dots after IV administration in F344/N rats." *Toxicologic Pathology.* **35**(1): 185-186.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300053

Cimon, K. Y., **D. E. Malarkey** and R. A. Miller (2007). "Incidences of mesenchymal neoplasms in the nasal cavity in NTP rodent studies." *Toxicologic Pathology.* **35**(1): 180-180.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300027

Clayton, N., K. Yoshizawa, **T. Burka, G. Kissling, P. C. Chan** and A. Nyska (2007). "Hepatocellular hypertrophy induced by oral treatment with kava extract in F344 rats: Immunohistochemical analysis of expressions of hepatic cytochrome P450." *Toxicologic Pathology.* **35**(1): 186-187.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300057

Clayton, N. P., K. Yoshizawa, **G. E. Kissling, L. T. Burka, P. C. Chan** and A. Nyska (2007). "Immunohistochemical analysis of expressions of hepatic cytochrome P450 in F344 rats following oral treatment with kava extract." *Exp Toxicol Pathol.* **58**(4): 223-36.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=17059882

Demchuk, E., B. Yucesoy, V. J. Johnson, M. Andrew, A. Weston, **D. R. Germolec**, C. T. De Rosa and M. I. Luster (2007). "A statistical model for assessing genetic susceptibility as a risk factor in multifactorial diseases: Lessons from occupational asthma." *Environmental Health Perspectives.* **115**(2): 231-234.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000243946800031

Flagler, N. D., **E. Ney, B. W. Mahler** and **R. R. Maronpot** (2007). "Image ethics: To adjust or not to adjust." *Toxicologic Pathology.* **35**(1): 197-197.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300101

Flagler, N. D., **E. Ney, B. W. Mahler** and **R. R. Maronpot** (2007). "Publication images: The good, the bad, and the impossible." *Toxicologic Pathology.* **35**(1): 197-197.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300102

Golomb, E., A. Schneider, E. Houminer, **J. Dunnick, G. E. Kissling**, J. Borman, A. Nyska and H. Schwalb (2007). "Bis(2-chloroethoxy) methane impairs cardiac mitochondrial response to ischemic injury; Ex vivo assessment of the functional mitochondrial effect of a cardiotoxic agent." *Toxicologic Pathology.* **35**(1): 195-195.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300094

Heinloth, A. N., **G. A. Boorman**, J. F. Foley, N. D. Flagler and R. S. Paules (2007). "Gene expression analysis offers unique advantages to histopathology in liver biopsy evaluations." *Toxicol Pathol.* **35**(2): 276-83.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=17366322

Johnson, **K. A., B. Mahler**, H. Y. Cho, S. R. Kleeberger and **R. R. Maronpot** (2007). "Structural model of hyperoxic lung injury in mice using micro-CT." *Toxicologic Pathology.* **35**(1): 183-183.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300043

Kirkland, D., S. Pfuhler, D. Tweats, M. Aardema, R. Corvi, F. Darroudi, A. Elhajouji, H. Glatt, P. Hastwell, M. Hayashi, P. Kasper, S. Kirchner, A. Lynch, D. Marzin, D. Maurici, J. R. Meunier, L. Muller, G. Nohynek, J. Parry, E. Parry, V. Thybaud, **R. Tice**, J. van Benthem, P. Vanparys and P. White (2007). "How to reduce false positive results when undertaking in vitro genotoxicity testing and thus avoid unnecessary follow-up animal tests: Report of an ECVAM Workshop." *Mutation Research-Genetic Toxicology and Environmental Mutagenesis.* **628**(1): 31-55.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000245320900004

Kodavanti, U., A. Nyska, A. Ledbetter, M. Schladweiler, R. Gottipolu, G. Wallenborn, R. Thomas, R. Jaskot, J. Richards, K. Crissman, G. Hatch, **G. Kissling** and **R. Maronpot** (2007). "Cardiovascular diseases, susceptibility to oxidative injury and compensatory mechanisms: Insights from rodent models." *Toxicologic Pathology.* **35**(1): 195-196.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300096

Melnick, R. L., A. Nyska, **P. M. Foster, J. H. Roycroft** and **G. E. Kissling** (2007). "Toxicity and carcinogenicity of the water disinfection byproduct, dibromoacetic acid, in rats and mice." *Toxicology.* **230**(2-3): 126-36.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=17157429

Mori, K., P. E. Blackshear, E. K. Lobenhofer, J. S. Parker, **D. P. Orzech, J. H. Roycroft**, K. L. Walker, K. A. Johnson, T. A. Marsh, **R. D. Irwin** and **G. A. Boorman** (2007). "Hepatic transcript levels for genes coding for enzymes associated with xenobiotic metabolism are altered with age." *Toxicol Pathology.* 35(2): 242-51.
http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=17366318

Newbold, R. R., E. Padilla-Banks, R. J. Snyder, T. M. Phillips and W. N. Jefferson (2007). "Developmental exposure to endocrine disruptors and the obesity epidemic." *Reprod Toxicol.* **23**(3): 290-6.
http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=17321108

Phillips, J. M., Y. Yamamoto, M. Negishi, **R. R. Maronpot** and J. I. Goodman (2007). "Orphan nuclear receptor constitutive active/androstane receptor-mediated alterations in DNA methylation during phenobarbital promotion of liver tumorigenesis." *Toxicological Sciences.* **96**(1): 72-82.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244262900009

Ramot, Y., D. Lewis, T. Ortel, G. Moser, M. Streiker, S. Ward, **S. Elmore**, S. Peddada and A. Nyska (2007). "Age and dose sensitivities in 2-butoxyethanol F344 rat model of hemdytic anemia and disseminated thrombosis." *Toxicologic Pathology.* **35**(1): 184-184.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300047

Sells, D. M., A. E. Brix, A. Nyska, M. P. Jokinen, **D. P. Orzech** and **N. J. Walker** (2007). "Respiratory tract lesions in noninhalation studies." *Toxicologic Pathology.* **35**(1): 170-177.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300020

Singh, B. P., P. R. Bushel and **D. E. Malarkey** (2007). "Correlation of transcriptome profiles and histologic alterations for seven known rodent hepatotoxicants." *Toxicologic Pathology.* **35**(1): 193-193.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300084

Ton, T. V., H. H. Hong, T. R. Devereux, **R. L. Melnick, R. C. Sills** and Y. Kim (2007). "Evaluation of genetic alterations in cancer-related genes in lung and brain tumors from B6C3F1 mice exposed to 1,3-butadiene or chloroprene." *Chem Biol Interact.* **166**(1-3): 112-20.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16860786

Travlos, G. S., L. Betz and G. C. Hard (2007). "The influence of diet or route of exposure on chronic progressive nephropathy, kidney weight, blood urea nitrogen and creatinine concentrations in 13-week toxicity studies for control F344/N male rats." *Toxicologic Pathology.* **35**(1): 190-191.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300074

Tweats, D. J., D. Blakey, R. H. Heflich, A. Jacobs, S. D. Jacobsen, T. Morita, T. Nohmi, M. R. O'Donovan, Y. F. Sasaki, T. Sofuni and **R. Tice** (2007). "Report of the IWGT working group on strategies and interpretation of regulatory *in vivo* tests - I. Increases in micronucleated bone marrow cells in rodents that do not indicate genotoxic hazards." Mutation Research-Genetic Toxicology and Environmental Mutagenesis. 627(1): 78-91.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244081300008

Tweats, D. J., D. Blakey, R. H. Heflich, A. Jacobs, S. D. Jacobsen, T. Morita, T. Nohmi, M. R. O'Donovan, Y. F. Sasaki, T. Sofuni and **R. Tice** (2007). "Report of the IWGT working group on strategy/interpretation for regulatory in vivo tests - II. Identification of *in vivo*-only positive compounds in the bone marrow micronucleus test." *Mutation Research-Genetic Toxicology and Environmental Mutagenesis.* **627**(1): 92-105.
http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244081300009

(Continued on page 10)

Tweats, D. J., D. Blakey, R. H. Heflich, A. Jacobs, S. D. Jacobsen, T. Morita, T. Nohmi, M. R. O'Donovan, Y. F. Sasaki, T. Sofuni and **R. Tice** (2007). "Report of the IWGT working group on strategies and interpretation of regulatory in vivo tests. I. Increases in micronucleated bone marrow cells in rodents that do not indicate genotoxic hazards." *Mutation Research - Genetic Toxicology and Environmental Mutagenesis.* **627**(1): 78-91. http://www.scopus.com/scopus/inward/record.url?eid=2-s2.0-33846186786&partnerID=40&rel=R6.0.0

Walker, N. J. (2007). "Unraveling the complexities of the mechanism of action of dioxins." *Toxicological Sciences.* **95**(2): 297-299. http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000243787800001

Wancket, L. M., J. P. Davis, B. D. Guenther, G. L. Woznicki, B. W. Johnson, B. D. Wahlstrand and **R. R. Maronpot** (2007). "Monitoring growth of DEN-induced mouse liver tumors using magnetic resonance microscopy (MRM)." *Toxicologic Pathology.* **35**(1): 194-194. http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300089

Weber, H. A., A. E. Hodges, J. R. Guthrie, B. M. O'Brien, D. Robaugh, A. P. Clark, R. K. Harris, J. W. Algaier and **C. S. Smith** (2007). "Comparison of proanthocyanidins in commercial antioxidants: Grape seed and pine bark extracts." *Journal of Agricultural and Food Chemistry.* **55**(1): 148-156. http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000243195000020

Woods, C. G., A. M. Burns, A. Maki, B. U. Bradford, **M. L. Cunningham**, H. D. Connor, M. B. Kadiiska, R. P. Mason, J. M. Peters and I. Rusyn (2007). "Sustained formation of alpha-(4-pyridyl-1-oxide)-N-tert-butylnitrone radical adducts in mouse liver by peroxisome proliferators is dependent upon peroxisome proliferator-activated receptor-alpha, but not NADPH oxidase." *Free Radical Biology and Medicine.* **42**(3): 335-342. http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000243764500003

Wyrobek, A. J., J. J. Mulvihill, J. S. Wassom, H. V. Malling, **M. D. Shelby**, S. E. Lewis, **K. L. Witt**, R. J. Preston, S. D. Perreault, J. W. Allen, D. M. DeMarini, R. P. Woychik, **J. B. Bishop**, D. Anderson, N. Arnheim, J. D. Boice, B. A. Bridges, J. F. Crow, Y. E. Dubrova, U. Eichenlaub-Ritter, R. P. Erickson, J. Fridlyand, J. Gray, P. C. Hanawalt, M. A. Handel, F. Marchetti, H. W. Mohrenweiser, R. K. Moyzis, M. Primig, L. B. Russell, K. Sankaranarayanan, M. K. Skinner, E. A. Shoubridge, J. A. Taylor, J. M. Trasler and T. J. Vasicek (2007). "Assessing human germ-cell mutagenesis in the postgenome era: A celebration of the legacy of William Lawson (Bill) Russell." *Environmental and Molecular Mutagenesis.* **48**(2): 71-95. http://www.scopus.com/scopus/inward/record.url?eid=2-s2.0-33847673752&partnerID=40&rel=R6.0.0

Yoshizawa, K., **N. J. Walker**, M. P. Jokinen, A. E. Brix, D. M. Sells, A. Nyska and **M. E. Wyde** (2007). "Thyroid follicular lesions induced by oral treatment for two years with 2,3,7,8-tetrachlorodibenzo-p-dioxin and dioxin-like compounds in female harlan Sprague-Dawley rats." *Toxicologic Pathology.* **35**(1): 194-195. http://gateway.isiknowledge.com/gateway/Gateway.cgi?&GWVersion=2&SrcAuth=CustomerName&SrcApp=CustomerName&DestLinkType=FullRecord&DestApp=WOS&KeyUT=ISI:000244891300091

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NTP Interagency Center for the Evaluation of Alternative Toxicology Methods (NICEATM)

alone assay for determining potency (including severity) for the purpose of hazard classification; (2) the "cut-down" or "limit dose" LLNA approach; (3) non-radiolabeled LLNA methods; (4) the use of the LLNA for testing mixtures, aqueous solutions, and metals; and (5) the current applicability domain (i.e., the types of chemicals and substances for which the LLNA has been validated). On May 17, 2007, NICEATM published a request for public comments on the on the appropriateness and relative priority of the nominated activities (72 FR 27815). NICEATM also requested the nominations of scientists with relevant knowledge and experience to serve on a panel if a meeting occurs and invited the submission of relevant data on LLNA. The nomination, public comments received, and additional information may be viewed on the NICEATM/ICCVAM web site http://iccvam.niehs.nih.gov/methods/immunotox/immunotox.htm

Request for Data on the Use of Topical Anesthetics and Systemic Analgesics for *In Vivo* Eye Irritation Testing

NICEATM and ICCVAM requested the submission of data and information on the use of topical anesthetics and systemic analgesics for alleviating pain and distress in rabbits during eye irritation testing. They also invited the submission of information about other procedures and strategies that may reduce or eliminate pain and distress associated with *in vivo* eye irritation methods (72 FR 26396). Comments and information relevant to this request are available on the NICEAMT/ICCVAM web site ● http://iccvam.niehs.nih.gov/methods/ocutox/pretreat.htm

Contact Information: Dr. William S. Stokes, Director, NICEATM, NIH/NIEHS, P.O. Box 12233, MD EC-32, Research Triangle Park, NC 27709; T: (919) 541-2384; FAX: (919) 541-0947; iccvam@niehs.nih.gov